

Please insert in its place the following:

This application is a divisional of U.S. application number 08/878,801, filed June 19 1997, now issued as U.S. Patent No. 6,004,808, which claims priority under 35 U.S.C. 119(e) to provisional patent application 60/020234 filed June 21, 1996, and to which it is a continuation in part, both of which are herein incorporated by reference.--

**IN THE CLAIMS**

Please cancel claim 1, and add new claims 63 to 109 as below.

--63. A method of identifying a G-protein coupled receptor (GPCR) for a given ligand, the method comprising:

- i) expressing a putative GPCR in a cell, said cell comprising,
- a) a first heterologous promoter operably linked to a first polynucleotide encoding G $\alpha$ 15 protein,
  - b) a second heterologous promoter operably linked to a second polynucleotide encoding a reporter gene,
- wherein said cell expresses said G $\alpha$ 15 protein at sufficient levels to permit promiscuous coupling to said GPCR, and wherein said second heterologous promoter is directly or indirectly modulated by the activity of said G $\alpha$ 15 protein,
- ii) contacting said cell with said ligand; and
- iii) detecting reporter gene expression.

64. The method of claim 63 wherein said cell comprises a third heterologous promoter operably linked to a third polynucleotide encoding said GPCR.

65. The method of claim 63, wherein said GPCR is not naturally expressed in said cell.

66. The method of claim 63, wherein said GPCR is a taste receptor.
67. The method of claim 66, further comprising contacting said cell with a reporter gene substrate.
68. The method of claim 63, further comprising contacting said cell with a compound that increases calcium levels inside said cell.
69. The method of claim 68, wherein said compound is selected from the group consisting of ionomycin and thapsigargin.
70. The method of claim 68, further comprising contacting said cell with phorbol myristate acetate or an analog thereof.
71. A method for identifying a GPCR for a given ligand, the method comprising:
- i) expressing a putative GPCR in a cell, said cell comprising, a first heterologous promoter operably linked to a first polynucleotide encoding  $G\alpha_{15}$  protein, wherein said cell stably expresses said  $G\alpha_{15}$  protein at sufficient levels to permit promiscuous coupling to said GPCR and wherein said GPCR is substantially coupled to either  $G\alpha_i$ ,  $G\alpha_s$  or  $G\alpha_{12}$  in the absence of said  $G\alpha_{15}$  protein;
  - ii) contacting said cell with said ligand; and
  - iii) detecting a signal with a signal transduction detection system, wherein said signal transduction detection system comprises a dye.
72. The method of claim 71 wherein said cell comprises a second heterologous promoter operably linked to a second polynucleotide encoding said GPCR.

73. The method of claim 71, wherein said GPCR is not naturally expressed in said cell.
74. The method of claim 71, wherein said signal transduction detection system comprises an intracellular calcium indicator.
75. A method of identifying of a ligand for a GPCR, the method comprising:  
i) contacting a cell with a test chemical, said cell comprising  
a first heterologous promoter operably linked to a first polynucleotide encoding  
G $\alpha$ 15 protein  
wherein said cell stably expresses said G $\alpha$ 15 protein at sufficient levels to  
permit promiscuous coupling to said GPCR and wherein said GPCR is  
substantially coupled to either G $\alpha_i$ , G $\alpha_s$  or G $\alpha_{12}$  in the absence of said  
G $\alpha$ 15 protein;  
ii) detecting a signal with a signal transduction detection system,  
wherein said signal transduction detection system comprises a dye.
76. The method of claim 75 wherein said cell further comprises a second heterologous promoter operably linked to a second polynucleotide encoding a GPCR.
77. The method of claim 76, wherein said GPCR is not naturally expressed in said cell.
78. The method of claim 75, wherein said signal transduction detection system comprises an intracellular calcium indicator.

79. The method of claim 75, further comprising comparing a signal from a first plurality of cells in the presence of said test chemical with either:

- sub 24
- i) a signal from a second plurality of cells in the presence of said test chemical, wherein said second plurality of cells lack either a promiscuous G $\alpha$  protein, a target protein, or
  - ii) a signal from a plurality of cells in the absence of said test chemical, wherein said plurality of cells are substantially the same as said first plurality of cells.

80. The method of claim 75, wherein said detecting comprises fluorescence detection.

81. A method of identifying a ligand for a GPCR, the method comprising

- sub 25
- i) contacting a cell with a test chemical, said cell comprising,
    - a) a first heterologous promoter operably linked to a first polynucleotide encoding G $\alpha$ 15 protein,
    - b) a second heterologous promoter operably linked to a second polynucleotide encoding a reporter gene,wherein said cell expresses said G $\alpha$ 15 protein at sufficient levels to permit promiscuous coupling to said GPCR, and wherein said second heterologous promoter is directly or indirectly modulated by the activity of said G $\alpha$ 15 protein;
  - ii) detecting reporter gene expression.
- B2

82. The method of claim 81 wherein said cell comprises a third heterologous promoter operably linked to a third polynucleotide encoding said GPCR.

83. The method of claim 81, wherein said GPCR is not naturally expressed in said cell.

84. The method of claim 81, wherein said detecting comprises fluorescence detection.
85. The method of claim 81, further comprising contacting said cell with a reporter gene substrate.
86. The method of claim 81, further comprising contacting said cell with a compound that increases calcium levels inside said cell.
87. The method of claim 86, wherein said compound is selected from the group consisting of ionomycin and thapsigargin.
88. The method of claim 81, further comprising contacting said cell with phorbol myristate acetate or an analog thereof.
89. The method of claim 81, further comprising comparing a signal from a first plurality of cells in the presence of said test chemical with either:
- i) a signal from a second plurality of cells in the presence of said test chemical, wherein said second plurality of cells lack either a promiscuous  $G\alpha$  protein, a target protein, or
  - ii) a signal from a plurality of cells in the absence of said test chemical, wherein said plurality of cells are substantially the same as said first plurality of cells.
90. A method for identifying a modulator of signal transduction in a cell, the method comprising:
- a) contacting a cell with a test chemical, said cell comprising a first heterologous promoter operably linked to a first polynucleotide encoding  $G\alpha 15$  protein, wherein said cell stably expresses said  $G\alpha 15$  protein at sufficient levels to permit promiscuous coupling to said GPCR and wherein said GPCR is

substantially coupled to either  $G\alpha_i$ ,  $G\alpha_s$  or  $G\alpha_{12}$  in the absence of said  $G\alpha_{15}$  protein;

- sub  
66  
Chil'd
- b) contacting said cell with a ligand that, in the absence of the test chemical, activates signal transduction in said cell, and
  - c) detecting a signal with a signal transduction detection system.

91. The method of claim 90 wherein said cell further comprises a second heterologous promoter operably linked to a second polynucleotide encoding a GPCR.
92. The method of claim 90, wherein said GPCR is not naturally expressed in said cell.
93. The method of claim 90, wherein said signal transduction detection system comprises an intracellular calcium indicator.
- B<sup>2</sup>
94. A method for identifying a modulator of signal transduction in a cell, the method comprising:
- i) contacting a cell with a test chemical, said cell comprising,
    - a) a first heterologous promoter operably linked to a first polynucleotide encoding  $G\alpha_{15}$  protein,
    - b) a second heterologous promoter operably linked to a second polynucleotide encoding a reporter gene,wherein said cell expresses said  $G\alpha_{15}$  protein at sufficient levels to permit promiscuous coupling to said GPCR, and wherein said second heterologous promoter is directly or indirectly modulated by the activity of said  $G\alpha_{15}$  protein,
  - ii) contacting said cell with a test chemical; and
  - iii) detecting reporter gene expression.
- sub  
B7  
C9

- B<sup>2</sup>
95. The method of claim 94 wherein said cell comprises a third heterologous promoter operably linked to a third polynucleotide encoding said GPCR.
96. The method of claim 94, wherein said GPCR is not naturally expressed in said cell.
97. The method of claim 94, wherein said detecting comprises fluorescence detection.
98. The method of claim 94, further comprising contacting said cell with a reporter gene substrate.
99. The method of claim 94, further comprising contacting said cell with a compound that increases calcium levels inside said cell.
100. The method of claim 99, wherein said compound is selected from the group consisting of ionomycin and thapsigargin.
101. The method of claim 94, further comprising contacting said cell with phorbol myristate acetate or an analog thereof.
102. A method of functionally profiling a test chemical comprising the steps of:
- i) contacting a panel of cells with a test chemical, said panel of cells comprising, a plurality of cell clones, each cell clone comprising
    - a) a GPCR,
    - b) a first heterologous promoter operably linked to a first polynucleotide encoding G $\alpha$ 15 protein,
    - c) a second heterologous promoter operably linked to a second polynucleotide encoding a reporter gene,
- pub  
B<sup>2</sup> C8

Sub  
68  
art'd

wherein said cell expresses said Gα15 protein at sufficient levels to permit promiscuous coupling to said GPCR, wherein said second heterologous promoter is directly or indirectly modulated by the activity of said Gα15 protein, and wherein each cell clone differs only with respect to the GPCR that is expressed,

- ii) contacting said cell clones with a test chemical;
- iii) detecting reporter gene expression from said cell clones
- iv) comparing reporter gene expression between said cell clones.

- B2  
July 14
103. The method of claim 102 wherein said cell clone comprises a third heterologous promoter operably linked to a third polynucleotide encoding said GPCR.
104. The method of claim 102, wherein said GPCR is not naturally expressed in said cell.
105. The method of claim 102, wherein said detecting comprises fluorescence detection.
106. The method of claim 102, further comprising contacting said cell with a reporter gene substrate.
107. The method of claim 102, further comprising contacting said cell with a compound that increases calcium levels inside said cell.
108. The method of claim 107, wherein said compound is selected from the group consisting of ionomycin and thapsigargin.
109. The method of claim 107, further comprising contacting said cell with phorbol myristate acetate or an analog thereof.--